

### REMARKS

In accordance with the present invention, there are provided genes encoding neuronal nicotinic acetylcholine receptor subunits and proteins encoded thereby. In particular, the invention relates to a family of novel mammalian neuronal nicotinic acetylcholine receptor subunits, for example, the beta2 subunit, which is a non-agonist binding subunit. The invention receptor subunit genes and the protein encoded thereby can be used for a variety of applications, *e.g.*, for drug design and screening. Moreover, the transformed cell lines expressing specific receptor subunits can be produced in quantity for reproducible quantitative analysis of the effects of drugs on receptor functions.

Claims 7, 34, 36, 37, 39 and 42 are amended herein. These amendments do not introduce new matter as they are fully supported throughout the specification and claims as originally filed. Claims 7 and 34-44 are pending. The specification and Figures of the instant application are amended herein to comply with the drawing requirements of 37 C.F.R. §1.84(U)(1). A clean copy of the Replacement Specification is provided herein as Appendix A, and a marked up copy of the Replacement Specification is provided herein as Appendix B. Table 1, below, provides a correlation between the numbering of the Figures as originally filed and the numbering of the Figures as amended herein.

**Table 1**

Figure # as originally filed.	Figure # as amended herein.
<b>1</b>	<b>1</b>
<b>2A-1</b>	<b>2A</b>
<b>2A-2</b>	<b>2B</b>
<b>2A-3</b>	<b>2C</b>
<b>2B-1</b>	<b>3A</b>
<b>2B-2</b>	<b>3B</b>
<b>2B-3</b>	<b>3C</b>
<b>3A</b>	<b>4A</b>
<b>3B</b>	<b>4B</b>

<b>4A</b>	<b>5A</b>
<b>4B</b>	<b>5B</b>
<b>5A</b>	<b>6A</b>
<b>5B</b>	<b>6B</b>
<b>6A</b>	<b>7A</b>
<b>6B</b>	<b>7B</b>
<b>7A</b>	<b>8</b>
<b>7B-1</b>	<b>9A</b>
<b>7B-2</b>	<b>9B</b>
<b>7B-3</b>	<b>9C</b>
<b>8</b>	<b>10</b>
<b>9A</b>	<b>11A</b>
<b>9B</b>	<b>11B</b>
<b>10A</b>	<b>12A</b>
<b>10B</b>	<b>12B</b>
<b>11</b>	<b>13</b>
<b>12</b>	<b>14</b>
<b>13A</b>	<b>15A</b>
<b>13B</b>	<b>15B</b>
<b>13C</b>	<b>15C</b>
<b>14A</b>	<b>16A</b>
<b>14B</b>	<b>16B</b>
<b>14C</b>	<b>16C</b>
<b>14D</b>	<b>16D</b>
<b>15A</b>	<b>17A</b>
<b>15B</b>	<b>17B</b>
<b>15C-1</b>	<b>18A</b>
<b>15C-2</b>	<b>18B</b>

<b>15C-3</b>	<b>18C</b>
<b>16</b>	<b>19</b>
<b>17A</b>	<b>20A</b>
<b>17B</b>	<b>20B</b>
<b>18A</b>	<b>21A</b>
<b>18B</b>	<b>21B</b>
<b>19A</b>	<b>22A</b>
<b>19B</b>	<b>22B</b>
<b>19C</b>	<b>22C</b>
<b>20</b>	<b>23</b>
<b>21</b>	<b>24</b>
<b>22</b>	<b>25</b>
<b>23</b>	<b>26</b>
<b>24A</b>	<b>27A</b>
<b>24B</b>	<b>27B</b>
<b>24C</b>	<b>27C</b>
<b>25A</b>	<b>28A</b>
<b>25B</b>	<b>28B</b>
<b>25C</b>	<b>28C</b>
<b>26</b>	<b>29</b>
<b>27</b>	<b>30</b>
<b>28</b>	<b>31</b>
<b>29</b>	<b>32</b>

**Drawings**

The objection to the figures as allegedly failing to meet the requirements of 37 C.F.R. §1.84(U)(1) has been obviated by the prior submission of replacement figures (with Applicant's communication dated 10/3/02). The revised figure numbers have been incorporated throughout the replacement specification submitted herewith. Reconsideration and withdrawal of this objection are respectfully requested.

**Claim 7**

The objection to claim 7 as allegedly not complying with 37 C.F.R. §1.84(U)(1) has been obviated by the amendments to the claims submitted herewith. Reconsideration and withdrawal of this objection are respectfully requested.

**Claims 35 and 38**

The objection to claims 35 and 38 as allegedly being of improper dependent form for failing to further limit the subject matter of claim 34 has been obviated by the amendments to claim 34 submitted herewith. As amended, claim 34 is directed to "A substantially pure polynucleotide or complement thereof...", which places claims 35 and 38 in proper dependent form. Reconsideration and withdrawal of this objection are respectfully requested.

**Rejection Of Claim 35 Under 35 U.S.C. §112, First Paragraph**

The rejection of claim 35 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or which it is most nearly connected, to make and/or use the invention is respectfully submitted to be without merit. The Examiner's attention is directed to the assertion in the specification, on page 16, line 30 to page 17, line 27, that the eight deposited materials have been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure, and that all restrictions on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent. The specification also provides the ATCC Deposit Numbers (accession number) for the eight deposited materials; recites the name and address of the

depository; and the complete taxonomic description thereof. These same deposits are also referred to in several issued U.S. patents from which the present application claims priority. These representations have been made several times previously. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

**Rejection Of Claims 34 And 36-44 Under 35 U.S.C. § 112, First Paragraph**

The rejection of claims 34 and 36-44 under 35 U.S.C. § 112, first paragraph, as allegedly being drawn to subject matter lacking adequate written description in the specification, is respectfully traversed.

Applicants respectfully disagree with the Examiner's assertion that the presence of the functional limitations in claims 34 and 36-44 in the absence of a description of those structural or chemical features needed to provide the recited functions, constitutes nothing more than a wish to know the identity of any polynucleotide meeting the limitations of the claims. Applicants also disagree with the assertion that the description in the specification of a single species of polynucleotide belonging to a large genus of polynucleotides encompassed by these claims does not provide adequate written support for the claimed genus.

Contrary to the Examiner's assertion, Applicant's specification provides substantial written description of the biochemical features, including both structural and functional properties of invention beta2 subunits of neuronal nicotinic acetylcholine receptors. Claims 34 and 36-44 describe a genus of polynucleotides, encoding a beta2 subunit of nAChR by reference to both structural and functional features. For example, claim 34 characterizes the invention beta2 subunit of nAChR by reference to both its structure (*e.g.*, sequences having a defined level of homology with respect to Figure 9) and function (*e.g.*, various functional properties recited in the claims); claim 39 defines the invention beta2 subunit by reference to both its structure (*e.g.*, hybridizes to the sequence shown in Figure 9) and function (*e.g.*, various functional properties recited in the claims); and claim 42 defines the invention beta2 subunit by reference to both its structure (*e.g.*, sequence having a defined level of homology with respect to other nAChR subunits) and function (*e.g.*, various functional properties). It is respectfully submitted that the detailed structural and functional properties of the beta2 subunits of neuronal nicotinic acetylcholine

receptors given in the specification provides an adequate written description for the genus of polynucleotides encompassed by these claims.

**Rejection Of Claims 34-44 Under 35 U.S.C. § 112, First Paragraph**

The Office Action has rejected claims 34-44 under 35 U.S.C. § 112, first paragraph, as allegedly being drawn to subject matter lacking adequate written description in the specification. While not necessarily agreeing with the Action, in the interest of advancing prosecution to issuance, claims 34-44 have been amended herein to recite "64% sequence homology" and "50% amino acid sequence identity" which renders the rejection of these claims moot. Accordingly, reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph, is respectfully requested.

**Rejection Of Claims 34-44 Under 35 U.S.C. § 112, Second Paragraph**

The rejection of claims 34-44 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is respectfully traversed.

**Claims 34-44**

Applicants respectfully disagree with the Examiner's assertion that claims 34-44 are allegedly vague and indefinite because the term "beta2" is allegedly not defined in the instant specification as exclusive to a protein encompassed by the term "beta2", having that property or combination of properties, which is unique to beta2 subunit.

It is respectfully submitted that the term "beta2" is clear when read in light of the specification. The structure of the beta2 subunit is described by reference to original Figure 7 (now Figures 8, 9A, 9B and 9C) and the various functional properties cited in the claims are described throughout the specification. For example, the specification provides basis for characterizing the beta2 subunit as:

- i) being able to substitute for the muscle beta1 subunit in the formation of an acetylcholine receptor, but not being able to substitute for the gamma or delta subunit of a neuronal nicotinic acetylcholine receptor, on page 56, line 3 to page 58, line 3;
- ii) not binding acetylcholine, nicotine or analogs thereof, on page 79, line 16 to page 80, line 14;

iii) forming, in conjunction with an alpha3 or an alpha4 subunit, a neuronal nicotinic acetylcholine receptor that is blocked by bungarotoxin 3.1 but not by  $\alpha$ -bungarotoxin, on page 26, lines 1-10, and on page 76, line 1 to page 81, line 20; and

iv) forming, in conjunction with an alpha2 subunit, a neuronal nicotinic acetylcholine receptor that is not blocked by either bungarotoxin 3.1 or  $\alpha$ -bungarotoxin, on page 26, lines 11-15, and on page 76, line 1 to page 81, line 20. Accordingly, reconsideration and removal of this grounds of rejection are respectfully requested.

**Claims 36 and 37**

The Examiner's assertion that claims 36 and 37 are allegedly vague and indefinite because there is no antecedent basis for "the substantially pure DNA of claim 34" has been obviated by the amendments submitted herewith. Independent claim 34 is directed to "a substantially pure polynucleotide...." As amended herein, dependent claims 36 and 37 are directed to "the substantially pure polynucleotide of claim 34," and therefore, have antecedent basis in claim 34. Accordingly, reconsideration and withdrawal of this grounds of rejection are respectfully requested.

**Claims 39-41**

The Examiner's assertion that claims 39-41 are allegedly vague and indefinite for reciting "stringent conditions" has been obviated by the amendments submitted herewith. As amended herein, claims 39-41 do not recite the term "stringent conditions." Accordingly, reconsideration and withdrawal of this grounds of rejection are respectfully requested.

**Claims 42-44**

The Examiner's assertion that claims 42-44 are allegedly vague and indefinite for reciting "50% amino acid sequence identity", "44% amino acid sequence identity" and "64% amino acid sequence identity" as allegedly requires reference to one or more specific amino acid sequences is respectfully traversed.

As amended herein, claims 42-44 recite the Figure numbers which identify the amino acid sequences as found in the substitute specification. For example, claim 42 recites:

- “a) 50% amino acid sequence identity to neuronal nicotinic acetylcholine receptor alpha subunits selected from the group consisting of alpha2 (Figures 18(A), 18(B) and 18(C)), alpha3 (Figure 13), alpha4 (Figure 13) and alpha5 (Figures 28(A), 28(B) and 28(C));
- b) 44% amino acid sequence identity to a beta3 subunit of a neuronal nicotinic acetylcholine receptor (Figure 23); and
- c) 64% amino acid sequence identity to a beta4 subunit of a neuronal nicotinic acetylcholine receptor (Figures 27(A), 27(B) and 27(C)).”

Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

### CONCLUSION

In view of the above amendments and remarks, the present application is respectfully submitted to be in condition for allowance. Accordingly, reconsideration and favorable action with respect to the pending claims is respectfully requested. In the event any issues remain to be resolved in view of this communication, the Examiner is invited to contact the undersigned at the number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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By 

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Enclosures: Appendix A  
Appendix B